simultaneously with antigen in a single injection with the immunopotentiating effect of lipopolysaccharide given simultaneously and continuously with antigen for four weeks. The lipopolysaccharide and antigen given subcutaneously and continuously was carried out with an osmotic device. The device comprised a reservoir made of butyl rubber, an intermediate layer of sodium chloride solute, and an outer wall of cellulose acetate. The device is described in U.S. Pat. No. 3,995,631. The antigen used, tetanus toxoid, permitted the use of an in vivo assay, with neutralization of toxin, for measuring the immunopotentiating effect.

#### Detailed Description Text (15):

Nine\_groups of mice (7/group) were immunized with a constant dose of tetanus toxoid (0.1 Lf=0.3 .mu.g) mixed with graded doses of LPS. Five of the groups received the immunizing dose of LPS and antigen, or antigen alone by a single subcutaneous injection. The immunizing dose was administered to the other 4 groups for 4 weeks, 4W. Twenty-eight days after the initiation of immunization, all mice were bled for antitoxin titration. On day 33, 3 mice from each group were challenged with 20 or 50 minimum lethal doses of tetanus toxin, and on day 35, the remaining 4 mice from each group were challenged with 8, 20, 50 or 125 MLDs. The results for the immunopotentiationg effects of continuous administration of tetanus toxoid with or without lipopolysaccharide are given in Table 3. In the table, 4W means 4 weeks continuous administration with the osmotic device, Sc indicates subcutaneous, and Inj indicates injection.

### Detailed Description Text (22):

An absorbed Diphtheria <u>vaccine</u> was prepared so as to contain 50 Lf [150 .mu.g] of Diphtheria toxoid and AlPO.sub.4 eqivalent to 0.65 mg Al per ml. Fifty Lf of Diphtheria toxoid is the maximum total dose that is usually given to children. 0.65 mg Al is the usual dose of alum adjuvant in <u>vaccines</u>. The maximum dose of Al permitted by the FDA is 0.85 mg Al. This <u>vaccine</u> was listed in guinea pigs at two dose levels: undiluted and diluted 1/50 in saline, by injecting 1.0 ml subcutaneously. The lower dose of the <u>vaccine</u> was expected to barely protect the guinea pigs against the diluted challenge dose of toxin.

### Detailed Description Text (23):

For administration at a controlled and continuous rate, a soluble <u>vaccine</u> was prepared so as to contain 50 Lf of Diphtheria toxoid and 10 .mu.g LPS in 0.175 ml. This <u>vaccine</u> was also listed at two dose levels, undiluted and diluted 1/50 in saline.

### Detailed Description Text (24):

Six groups of guinea pigs (5/group) were used in this experiment. Four groups were immunized with the absorbed and the soluble (Toxoid+LPS) vaccine. The fifth group received 50 Lf toxoid alone at a controlled and continuous rate. The sixth group was used as a control. All the groups were bled on day 28 for antitoxin titration and skin tested with the toxin and the toxoid on day 29. Each of the immunized animals were given 4 skin tests as follows:

### Detailed Description Paragraph Table (5):

## CLAIMS:

14. The method for potentiating the immune response of the animal according to claim

# **WEST Search History**

DATE: Tuesday, February 04, 2003

| Set Name Query side by side                            |   | Hit Count | Set Name result set |
|--|---|-----------|---------------------|
| DB = USPT, PGPB, JPAB, EPAB, DWPI; PLUR = YES; OP = OR |   |           |                     |
| L18  | vaccine and (FHA and PT and diptheria and tetanus)                        | 10        | L18                 |
| L17  | L16 and (tetanus and diptheria and vaccine)                               | 29        | L17                 |
| L16  | (vaccine same ((multiple or plural) with antigen))                        | 483       | L16                 |
| $DB=USPT,PGPB,DWPI;\ PLUR=YES;\ OP=OR$                 |   |           |                     |
| L15  | L14 and 17  | 24        | L15                 |
| L14  | (vaccine and ((multiple or plural) same antigen)) AnD ((@pd > 20020426)!) | 1021      | L14                 |
| L13  | (L10) AnD ((@pd > 20020426)!)   | 85        | L13                 |
| L12 .  | (L11) AnD ((@pd > $20020426$ )!)  | 0         | L12                 |
| DB=USPT; $PLUR=YES$ ; $OP=OR$                          |   |           |                     |
| L11  | (L10 and L4) AnD ((@pd > 20020426)!)                                      | 0         | L11                 |
| L10  | (multivalent same vaccine) AnD ((@pd > 20020426)!)                        | 85        | L10                 |
| L9   | (L4 and L7) AnD ((@pd > 20020426)!)                                       | 0         | L9                  |
| L8   | (L6 and L7) AnD ((@pd > 20020426)!)                                       | 5         | L8                  |
| L7   | (tetanus and diptheria and pertussis) AnD ((@pd > 20020426)!)             | 39        | L7                  |
| L6   | (trivalent or multivalent adj10 vaccine) AnD ((@pd > 20020426)!)          | 933       | L6                  |
| L5   | (L3 and L4) AnD ((@pd > 20020426)!)                                       | 0         | L5                  |
| L4   | ((hepatitus same B) and vaccine) AnD ((@pd > 20020426)!)                  | 6         | L4                  |
| L3   | (L1 and L2) AnD ((@pd > 20020426)!)                                       | 36        | L3                  |
| L2   | (tetanus and diptheria and vaccine) AnD ((@pd > 20020426)!)               | 40        | L2                  |
| L1   | ((pertussis or 69K or pertactin) and vaccine) AnD ((@pd > 20020426)!)     | 158       | L1                  |

END OF SEARCH HISTORY